



CLAIMS

(original) An immunostimulatory nucleic acid molecule having at least one internal pyrimidine-purine (YZ) dinucleotide and a chimeric backbone, wherein the at least one internal YZ dinucleotide has a phosphodiester or phosphodiester-like internucleotide linkage, wherein optionally each additional internal YZ dinucleotide has a phosphodiester, phosphodiester-like, or stabilized internucleotide linkage, and wherein all other internucleotide linkages are stabilized.

2. (original) The oligonucleotide of claim 1, wherein the immunostimulatory nucleic acid comprises a plurality of internal YG dinucleotides having a phosphodiester or phosphodiester-like internucleotide linkage.

3. (withdrawn) The oligonucleotide of claim 2, wherein every internal YG dinucleotide has a phosphodiester or phosphodiester-like internucleotide linkage.

4. (withdrawn) The oligonucleotide of claim 1, wherein the immunostimulatory nucleic acid molecule is any one of SEQ ID NO:1 – 54, SEQ ID NO:55-99 and SEQ ID NO:241, wherein * shown in the SEQ ID No's in the specification represents phosphorothioate, _ represents phosphodiester, U represents 2'-deoxyuracil; and 7 represents 7-deazaguanine.

5. (withdrawn) The oligonucleotide of claim 1, wherein the immunostimulatory nucleic acid molecule is selected from the group consisting of:

T*C_G*T*C_G*T*T*T_G*T*C_G*T*T*T_G*T*C_G*T*T (SEQ ID NO:100),
T*C_G*T*C_G*T*T*T_G*T*C_G*T*T (SEQ ID NO:101),
T*C_G*T*C_G*T*T*T_C_G*T*C_G*T*T (SEQ ID NO:102),
T*G*T*C_G*T*T*T_G*T*C_G*T*T_G*T*C_G*T*T (SEQ ID NO:103),
and T*C_G*T*C_G*T*T*T*T*C_G*G*G*C*G*G*C*C*G*C*C*G (SEQ ID NO:104),
wherein * represents phosphorothioate and _ represents phosphodiester.

6-11. (canceled)

12. (original) The oligonucleotide of claim 1, wherein the at least one internal YG dinucleotide having a phosphodiester or phosphodiester-like internucleotide linkage is CG.

13. (withdrawn) The oligonucleotide of claim 1, wherein the at least one internal YG dinucleotide having a phosphodiester or phosphodiester-like internucleotide linkage is TG.

14. (original) The oligonucleotide of claim 1, wherein the immunostimulatory nucleic acid molecule is a B-Class immunostimulatory nucleic acid molecule.

15. (withdrawn) The oligonucleotide of claim 1, wherein the immunostimulatory nucleic acid molecule is a C-Class immunostimulatory nucleic acid molecule.

16. (original) The oligonucleotide of claim 1, wherein the immunostimulatory nucleic acid molecule is 4-100 nucleotides long.

17. (original) The oligonucleotide of claim 1, wherein the immunostimulatory nucleic acid molecule is not an antisense oligonucleotide, triple-helix-forming oligonucleotide, or ribozyme.

18-21. (canceled)

22. (original) The oligonucleotide of claim 1 wherein the nucleic acid has a backbone comprising deoxyribose or ribose.

23. (withdrawn) The oligonucleotide of claim 1, wherein the oligonucleotide further comprises an adjuvant or a cytokine, or an antigen.

24. (original) The oligonucleotide of claim 1 wherein the phosphodiester or phosphodiester-like internucleotide linkage is phosphodiester.

25. (withdrawn) The oligonucleotide of claim 1 wherein the phosphodiester-like linkage is boranophosphonate or diastereomerically pure Rp phosphorothioate.

26. (original) The oligonucleotide of claim 1 wherein the stabilized internucleotide linkages are selected from the group consisting of: phosphorothioate, phosphorodithioate, methylphosphonate, methylphosphorothioate, and any combination thereof.

27. (original) The oligonucleotide of claim 1 wherein the stabilized internucleotide linkages are phosphorothioate.

28. (withdrawn) An oligonucleotide comprising:

5’T*C*G*T*CGTTTGAN₁CGN₂*T*T3’ (SEQ ID NO: 296)

wherein N₁ is 0-6 nucleotides and optionally is 0-2 nucleotides, wherein N₂ is 0-7 nucleotides, wherein * refers to the presence of a stabilized internucleotide linkage, and wherein the oligonucleotide includes at least 2 phosphodiester internucleotide linkages and optionally the oligonucleotide is 16-24 nucleotides in length.

29-31. (canceled)

32. (withdrawn) An oligonucleotide comprising:

5’ T*C*G*(T*/A*)TN₃CGTTTN₄CGN₅*T*T 3’ (SEQ ID NO: 301)

wherein N₃ is 0-4 nucleotides, wherein N₄ is 1-5 nucleotides and optionally is 1-2 nucleotide, wherein N₅ is 0-7 nucleotides, wherein * refers to the presence of a stabilized internucleotide linkage, and wherein the oligonucleotide includes at least 3 phosphodiester internucleotide linkages and optionally the oligonucleotide is 16-24 nucleotides in length.

33-35. (canceled)

36. (withdrawn) An oligonucleotide comprising:

5'T*C*G*T*C*GN_nCGNCGNNNC*G*N*C*G*T*T3' (SEQ ID NO: 306)

wherein N is any nucleotide, wherein * refers to the presence of a stabilized internucleotide linkage, and wherein the oligonucleotide includes at least 3 phosphodiester internucleotide linkages and optionally 5 phosphodiester internucleotide linkages and wherein the oligonucleotide optionally is 16-24 nucleotides in length.

37-38. (canceled)

39. (withdrawn) An oligonucleotide comprising:

5'T*CGCGN₈CGCGC*GN₉3' (SEQ ID NO: 315)

wherein N₈ is between 4 and 10 nucleotides in length and includes at least 1 C_G motif and optionally at least 2 or 3 CG motifs, wherein N₉ is between 0 and 3 nucleotides in length, wherein * refers to the presence of a stabilized internucleotide linkage, and wherein _ refers to the presence of a phosphodiester internucleotide linkage and wherein the oligonucleotide has a length of 15-40 nucleotides.

40-43. (canceled)

44. (original) An oligonucleotide comprising:

5'T*C_G(N₆C_G N₇)₂₋₃T*C_G*T*T3' (SEQ ID NOs: 311-312)

wherein N₆ and N₇ are independently between 1 and 5 nucleotides in length, and optionally N₆ is one nucleotide, preferably T or A and optionally N₇ is five nucleotides, preferably five pyrimidines or TTTTG wherein * refers to the presence of a stabilized internucleotide linkage, and wherein _ refers to the presence of a phosphodiester internucleotide linkage and wherein the oligonucleotide has a length of 16-40 nucleotides.

45. (canceled)

46. (withdrawn) An oligonucleotide comprising:

5'T*T*GX₁X₂TG X₃X₄T*T*T*T*N₁₀T*T*T*T*T*T3' (SEQ ID NO: 318)

wherein N₁₀ is between 4 and 8 nucleotides in length and includes at least 1 C_G motif and optionally includes at least 2 or 3 CG motifs, wherein X₁, X₂, X₃, and X₄ are independently C or G, wherein * refers to the presence of a stabilized internucleotide linkage, and wherein _ refers to the presence of a phosphodiester internucleotide linkage and wherein the oligonucleotide has a length of 24-40 nucleotides.

47. (canceled)

48. (withdrawn) An oligonucleotide comprising:

5' T*C*G*C_G*A*C*G*T*T*C_G*G*C_G*C_G*C*G 3' (SEQ ID NO: 321)

wherein * refers to the presence of a stabilized internucleotide linkage, and wherein _ refers to the presence of a phosphodiester internucleotide linkage and optionally wherein the oligonucleotide has a length of 21-40 nucleotides.

49. (original) An oligonucleotide comprising:

an octameric sequence comprising at least one YZ dinucleotide having a phosphodiester or phosphodiester-like internucleotide linkage, and at least 4 T nucleotides, wherein Y is a pyrimidine or modified pyrimidine, wherein Z is a guanosine or modified guanosine, and wherein the oligonucleotide includes at least one stabilized internucleotide linkage.

50-65. (canceled)

66. (original) An oligonucleotide comprising:

5' TCGTCGTTTGACGTTTGTGTT 3' (SEQ ID NO: 368)

wherein at least one CG dinucleotide has a phosphodiester or phosphodiester-like internucleotide linkage, and the oligonucleotide includes at least one stabilized internucleotide linkage.

67. (original) An oligonucleotide comprising:

5'GNC 3', wherein N is a nucleic acid sequence of 4-10 nucleotides in length and is at least 50% T and does not include a CG dinucleotide, and the oligonucleotide includes at least one stabilized internucleotide linkage.

68-69. (canceled)

70. (withdrawn) A method for modulating an immune response, comprising administering to a subject an oligonucleotide of claim 1, in an effective amount to modulate an immune response.

71-87. (canceled)

88. (withdrawn) A method for treating airway remodeling, comprising: administering to a subject an oligonucleotide comprising a CG dinucleotide, in an effective amount to treat airway remodeling in the subject.

89-93. (canceled)

94. (withdrawn) A method for stimulating an immune response, comprising administering to a subject an oligonucleotide of at least 5 nucleotides in length in an effective amount to stimulate an immune response, wherein the oligonucleotide includes at least one immunostimulatory dinucleotide motif wherein the internucleotide linkage between the nucleotides of the dinucleotide has R chirality and wherein at least 70% of the other internucleotide linkages of the oligonucleotide have S chirality.

95. (withdrawn) An oligonucleotide, comprising: an immunostimulatory nucleic acid molecule comprising a chimeric backbone and at least one sequence $N_1 YGN_2$, wherein independently for each sequence $N_1 YGN_2$ YG is an internal pyrimidine-guanosine (YG) dinucleotide, N_1 and N_2 are each, independent of the other, any nucleotide, and wherein for the at least one sequence $N_1 YGN_2$ and optionally for each additional sequence $N_1 YGN_2$:

the YG dinucleotide has a phosphodiester or phosphodiester-like internucleotide linkage, and

(a) N_1 and Y are linked by a phosphodiester or phosphodiester-like internucleotide linkage when N_1 is an internal nucleotide,

(b) G and N_2 are linked by a phosphodiester or phosphodiester-like internucleotide linkage when N_2 is an internal nucleotide, or

(c) N_1 and Y are linked by a phosphodiester or phosphodiester-like internucleotide linkage when N_1 is an internal nucleotide and G and N_2 are linked by a phosphodiester or phosphodiester-like internucleotide linkage when N_2 is an internal nucleotide, wherein all other internucleotide linkages are stabilized.

96. (withdrawn) An oligonucleotide comprising

$N_1-C-G-N_2-C-G-N_3$ (SEQ ID NO:389)

wherein N_1 and N_3 are each independently a nucleic acid sequence 1-20 nucleotides in length, wherein _ indicates an internal phosphodiester or phosphodiester-like internucleotide linkage, wherein N_2 is independently a nucleic acid sequence 0-20 nucleotides in length, and wherein G- N_2 -C includes 1 or 2 stabilized linkages.

97. (previously presented) An oligonucleotide comprising

$N_1-C-G-N_2-C-G-N_3$ (SEQ ID NO:390)

wherein N_1 and N_3 are each independently a nucleic acid sequence 1-20 nucleotides in length, wherein _ indicates an internal phosphodiester or phosphodiester-like internucleotide

linkage, wherein N₂ is independently a nucleic acid sequence 4-20 nucleotides in length, and wherein G-N₂-C includes at least 5 stabilized linkages.

98. (previously presented) An oligonucleotide comprising
N₁-C_G-N₂-C_G-N₃ (SEQ ID NO:391)

wherein N₁, N₂, and N₃ are each independently a nucleic acid sequence of 0-20 nucleotides in length and wherein _ indicates an internal phosphodiester or phosphodiester-like internucleotide linkage, wherein the oligonucleotide is not an antisense oligonucleotide, triple-helix-forming oligonucleotide, or ribozyme.

99. (withdrawn) An oligonucleotide comprising
X₁-N₁-(GTCGTT)_n-N₂-X₂ (SEQ ID NOs:18, 19, 20, and 57)

wherein N₁ and N₂ are each independently a nucleic acid sequence of 0-20 nucleotides in length, wherein n=2 or n=4-6, wherein X₁ and X₂ are each independently a nucleic acid sequence having phosphorothioate internucleotide linkages of 3-10 nucleotides, wherein N₁-(GTCGTT)_n-N₂ includes at least one phosphodiester internucleotide linkage, and wherein 3' and 5' nucleotides of the oligonucleotide do not include a poly-G, poly-A, poly-T, or poly-C sequence.

100. (previously presented) The oligonucleotide of claim 44, wherein the oligonucleotide has the following structure:

5' T*C_G*T*C_G*T*T*T*T*G*A*C_G*T*T*T*T*G*T*C_G*T*T 3' (SEQ ID NO: 313) or
5' T*C_G*A*C_G*T*T*T*T*G*T*C_G*T*T*T*T*G*T*C_G*T*T 3' (SEQ ID NO: 314).